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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
EPPERSON, JON D	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 05/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/801,157	JOSEL ET AL.	
	Examiner	Art Unit	
	Jon D Epperson	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) *18,25 and 32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17,19-24 and 26-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/20/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Request for Continued Examination (RCE)

1. A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/20/03 has been entered. Applicants' response on 3/4/2004 is also noted. Claims 1-8 were pending. Applicants amended claims 1-2 and 8. Applicants also added new claims 9-32. Therefore, claims 1-32 are currently pending. An action on the merit follows. Those sections of Title 35, US code, not included in the instant action can be found in previous office actions.

2. Please note: Applicant's elected species (e.g., see 3/4/2004 Response) were found in the art, see rejections below. Applicant is reminded of MPEP § 803.02 with respect to species elections:

> On the other hand, should no prior art be found that anticipates or renders obvious the elected species, the search of the Markush-type claim will be extended. If prior art is then found that anticipates or renders obvious the Markush-type claim with respect to a nonelected species, the Markush-type claim shall be rejected and claims to the nonelected species held withdrawn from further consideration. The prior art search, however, will not be extended unnecessarily to cover all nonelected species. Should applicant, in response to this rejection of the Markush-type claim, overcome the rejection, as by amending the Markush-type claim to exclude the species anticipated or rendered obvious by the prior art, the amended Markush-type claim will be reexamined. The prior art search will be extended to the extent necessary to determine patentability of the Markush-type claim. In the event prior art is found during the reexamination that anticipates or renders obvious the amended Markush-type claim, the claim will be rejected and the action made final. Amendments submitted after the final rejection further restricting the scope of the claim may be denied entry.

3. Claims 18, 25 and 32 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected species (see below i.e., ***Response to Restriction and/or Election of Species***).

4. Therefore, claims 1-17, 19-24 and 26-31 are examined on the merits.

Response to Restriction and/or Election of Species

5. Applicant's election of species Group I in the 3/4/2004 Response is acknowledged.

6. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election of species has been treated as an election without traverse (MPEP § 818.03(a) and/ or 37 CFR 1.111(b)).

7. As a result, the restriction requirement and/or election of species is still deemed proper and is therefore made FINAL.

Withdrawn Objections/Rejections

8. With respect to the rejections under the second paragraph of 35 U.S.C. 112, the rejections denoted C and G are withdrawn in view of applicant's amendments to the claims and/or cancellation of claims. The Crockford et al. rejection under 35 U.S.C. § 102(b) is withdrawn in

view of Applicant's amendments and/or arguments. All other rejections are maintained and the arguments are addressed below.

Outstanding Objections and/or Rejections

Claim Rejections - 35 USC § 112, First Paragraph

9. Claims 1,2, and 8 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed had possession of the claimed invention. This is a written description rejection.

To satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. Applicants' claims are directed to conjugates that are defined in "functional" terms. The claims use generic terminology such as "hapten," "marker group," "solid phase binding group," "reactive side groups," and "predetermined positions." These terms are set forth in the instant disclosure but the definitions are relative, broad and/or completely open-ended.

In *Enzo* (*Enzo Biochem, Inc. v. Gen-Probe Inc.*, 285 F.3d 1013 (Fed. Cir. 2002)), the court adopted the standard set forth in the Patent and Trademark Office ("PTO") Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, 1 "Written Description" Requirement ("Guidelines"), 66 Fed. Reg. 1099 (Jan. 5, 2001), which states that the written description requirement can be met by "showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics,"

including, *inter alia*, "functional characteristics ***when coupled with a known or disclosed correlation between function and structure*** ... ." *Enzo*, 296 F.3d at 1324-25 (quoting Guidelines, 66 Fed. Reg. at 1106 (emphasis added)). Here, Applicants have not provided any such "identifying characteristics" or "correlation between function and structure" that might otherwise render their claimed functional language permissible. Claims 1, 2 and 8 contain no structural information whatsoever for the "hapten molecules" and "marker groups" or "solid phase binding groups" and also no structural features for the linkages that connects them. The molecules/groups in question are infinite in scope possessing widely varying structures.

With respect to adequate disclosure of the scope of the presently claimed generic Applicants are also referred to the discussion in *University of California v. Eli Lilly and Co.* (U.S. Court of Appeals Federal Circuit (CAFC) 43 USPQ2d 1398 7/22/1997 Decided July 22, 1997; No. 96-1175). For adequate disclosure, like enablement, requires *representative examples* that provide reasonable assurance to one skilled in the art that the compounds falling within the scope both possess the alleged utility and additionally demonstrate that *applicant had possession of the* ***full scope*** *of the claimed invention.* See In re Riat et al. (CCPA 1964) 327 F2d 685, 140 USPQ 471; In re Barr et al. (CCPA 1971) 444 F 2d 349, 151 USPQ 724 (for enablement) and University *of California v. Eli Lilly and Co* cited above (for disclosure). The more unpredictable the art the greater the showing required (e.g. by "representative examples") for both enablement and adequate disclosure.

Here, the instant specification discloses only conjugates containing amino acid carriers with luminescent bi-pyridine metal chelate marker groups or biotin solid phase binging groups and small organic molecule haptens like testosterone that are attached through reactive amino groups (e.g., lysine amino group). Applicants' claimed scope represents only an invitation to experiment regarding other possible "haptens," "marker groups," "solid phase binding groups" and "reactive side groups." The claimed scope encompasses nucleotides and/or peptidic nucleic acids as the "polymeric carrier" which are also not sufficiently described in the instant specification. Thus the application fails to describe sufficient examples of conjugates that are within the scope of the presently claimed invention.

The CCPA held, "[T]he essential goal of the description of the invention requirement is to clearly convey the information that an applicant has invented the subject matter which is claimed." *In re Barker*, 559 F.2d 588, 592 n.4, 194 USPQ 470, 473 n.4 (CCPA 1977), cert. denied, 434 U.S. 1064 (1978). Another objective is to put the public in possession of what the applicant claims as the invention so that the public may ascertain if the patent applicant claims anything that is in common use, or already known. *Evans v. Eaton*, 20 U.S. (7 Wheat.) 356 (1822). In the present case, the disclosure is neither representative of the claimed genus nor does it represent a substantial portion of the claimed genus (see above). Thus, Applicants have not "clearly conveyed" that they are in possession of the full scope of the claimed method.

Response

10. Applicant's arguments directed to the above written description rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

[1] Applicants argue, "there is nothing inherently wrong with defining some part of the invention in functional terms" and cite *In re Swinehart* in support of this position (e.g., see 10/20/2003 Response, page 12, paragraph 3).

[2] Applicants argue, "hapten molecules," "marker groups," "solid phase binding groups" and "reactive side groups" were well known in the art and refer to exhibits A and B (e.g., see 10/20/2003 Response, page 12, paragraph 4).

[3] Applicants argue, "the claimed invention is not dependent upon-and, therefore, should not be limited to-specific types of 'hapten molecules,' 'marker groups,' 'solid phase binding groups' or 'reactive side groups.' (e.g., see 10/20/2003 Response, page 12, paragraph 4).

This is not found persuasive for the following reasons:

[1] The Examiner agrees that there is nothing "inherently" wrong with using functional terminology, but disagrees that Applicants' functional language meets the standards of written description in this case. The language of the specification should describe the claimed invention so that one skilled in the art can recognize what is claimed. A description of a compound in terms of its function fails to distinguish the compound from others having the same activity or function. A description of what a material does, rather than of what it is, ***usually does not***

suffice. The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter purportedly described. University of California v. Eli Lilly and Co. (U.S. Court of Appeals Federal Circuit (CAFC) 43 USPQ2d 1398 7/22/1997 Decided July 22, 1997; No. 96-1175).

Here, a person of skill in the art would not be able to "visualize" or "recognize" the identity of the infinite number of conjugates that are produced by the claimed methods. For example, what chemical "structures" would be encompassed by the term hapten? This question cannot be answered because "hapten" defines a product **solely** by its function (i.e., its ability to participate in an immune response), not by its structure. In addition, this problem is further exacerbated by Applicants' use of multiple functional terms (e.g., "marker groups", "solid phase binding groups", "reactive side groups") to form the structurally undefined conjugates. Applicants do not place any limitations on the structures of these groups/molecules or the ways in which they can be connected and, as a result, the must be determined on a "case-by-case" basis or "trial-and-error" basis (see Paper No. 9, page 7) wherein no other "identifying characteristics" or "structure/function correlations" are provided in violation of the Written Description Guidelines (e.g., See *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 285 F.3d 1013 (Fed. Cir. 2002)) wherein the court adopted the standard set forth in the Patent and Trademark Office ("PTO") Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, 1 "Written Description" Requirement ("Guidelines"), 66 Fed. Reg. 1099 (Jan. 5, 2001), which state that the written description requirement can be met by "showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics," including, *inter ali*a, "functional characteristics ***when coupled with a known or disclosed correlation between***

function and structure ... ." *Enzo*, 296 F.3d at 1324-25 (quoting Guidelines, 66 Fed. Reg. at 1106 (emphasis added))).

[2] The Examiner contends that the general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify all of the members of the genus or even a substantial portion thereof, and because the genus is enormous and highly variant, providing general references on fluorescence immunoassays and organic synthesis do not suffice because they do not provide any detailed information on how to produce the infinite number of claimed conjugates. Moreover, when there is little to no disclosure in the instant specification of the starting materials or conditions under which the claimed process can be carried out, this failure cannot be rectified by asserting that all disclosure related to the process is within the skill of the art. *Genentech Inc. v. Novo Nordisk A/S* (CA FC) 42 USPQ2d 1001 (3/13/1997).

[3] The Examiner respectfully disagrees. The claimed invention MUST depend on the hapten molecules, marker groups, solid-phase binding groups and reactive side groups because the claimed invention could not be practiced without them. Furthermore, a person of skill in the art would not know how to produce any particular conjugate without knowing the underlying chemical structure (e.g., hapten, marker, etc.) from which said conjugate is to be built. For example, a person that has a claim to produce a molecule that selectively inhibits a Cox-2 receptor (or immunological conjugates by analogy to the present case) really is not in possession of such a method if the molecule that is/are relied on to produce such an effect (inhibit Cox-2 receptors or act as immunological conjugates in the present case) is not known (e.g., see

University of Rochester v. G.D. Searle & Co., Inc., 358 F.3d 916, 926 (Fed.Cir.2004)). Furthermore, literature references that teach general methods for assays or organic synthesis do not alleviate this deficiency because the target molecule is not known and thus these general references do not supply the "specific guidance" that is required.

Accordingly, the written description rejection cited above is hereby maintained.

11. Claims 1-32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for producing conjugates that contain (a) monomeric amino acids units in the carrier and hapten molecules attached to (b) ruthenium bi-pyridine luminescent metal marker groups or (c) biotin solid-phase binding groups, does not reasonably provide enablement for the limitless number of conjugates that are currently claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include, but are not limited to:

(1) the breadth of the claims;
(2) the nature of the invention;
(3) the state of the prior art;
(4) the level of one of ordinary skill;
(5) the level of predictability in the art;
(6) the amount of direction provided by the inventor;
(7) the existence of working examples; and
(8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

See *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

(1-2) The breadth of the claims and the nature of the invention: The claims are drawn to conjugates that comprise a polymeric carrier that is made up of monomer units that are amino acids, nucleotides and/or peptidic nucleic acids. These conjugates further comprise "hapten molecules, " "marker groups" or "solid phase binding groups." These moieties are attached to the polymeric carrier via "reactive side groups" at "predetermined positions." Such represents very broad scope because these molecules and/or groups represent an infinite number of compounds.

(3 and 5) The state of the prior art and the level of predictability in the art: The process of preparing conjugates that comprise peptidic backbones that have certain specific "hapten molecules" and "marker groups or solid phase binding groups" attached thereto via "reactive side groups" are known in the art at the time of filing (see rejections below); however, only limited numbers of such conjugates were known and the specification gives no guidance to permit one of skill in the art to devise strategies for synthesis of conjugates with other types of backbones (e.g., sugar-phosphate backbone of DNA). The structures of possible variants are sufficiently diverse and one of ordinary skill would not be able to predict their structures.

For example, Riley et al. (e.g., see Riley, R. J.; Leeder, J. S. "In vitro analysis of metabolic predisposition to drug hypersensitivity" Clinical and Experimental Immunology 1995, 99(1), 1-6) disclose idiosyncratic hypersensitivity reactions (which may account for up to 25% of all adverse drug reactions) that are "unpredictable" in nature (see Riley et al., abstract). Riley et al. state, "[t]he multifactorial nature of hypersensitivity reactions, particularly the role of often ***unidentified***, reactive drug

metabolites [haptens] in antigen generation, has hampered the routine diagnosis of these disorders" (see Riley et al., abstract). In other words, Riley et al. specifically state that the identity and structure of many haptens associated with idiosyncratic hypersensitivity reactions have not be determined because these haptens represent metabolic intermediates that are difficult to isolate for physical characterization.

In addition, it is not clear whether a hapten will retain its functional properties when it is bound to a carrier. Will a hapten remain biologically active when bound to an oligomer with 100 alanine residues? Will that same hapten remain biologically active when bound to an oligomer with 10 adenines? A person of skill in the art would not be able to predict *a priori* the effects of linking a hapten to a carrier. The specification does not provide "direction and guidance of a more general nature" that would solve this problem.

(4) The level of one of ordinary skill: The level of skill required would be high, most likely at the Ph.D. level

(6-7) The amount of direction provided by the inventor and the existence of working examples: Applicants have provided only a limited number of examples including a conjugate containing an amino acid carrier (lysine derivative) with a luminescent ruthenium bi-pyridine metal chelate marker group (or biotin solid-phase binding group) and a small organic molecule hapten (e.g., testosterone) that are attached through reactive amino side groups. Thus, the teachings of the instant specification is quite limited.

(8) The quantity of experimentation needed to make or use the invention base on the content of the disclosure: As a result of the broad and unpredictable nature of the

invention and the lack of specific guidance from the specification, the Examiner contends that the quantity of experimentation needed to make and or use the invention would be great. Note that there must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and use the invention as broadly as it is claimed. *In re Vaeck*, 947 F.2d 488, 496 & n.23, 20 USPQ2d 1438, 1445 * n.23 (Fed. Cir. 19991). In this case, Applicants have not provided any working examples that would teach this enormous genus that falls within a highly unpredictable art area. Therefore, it is deemed that further research of an unpredictable nature would be necessary to make or use the invention as claimed. Thus, due to the inadequacies of the instant disclosure one of ordinary skill would not have a reasonable expectation of success and the practice of the full scope of the invention would require undue experimentation.

Response

12. Applicant's arguments directed to the above Enablement rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address Applicants' newly amended and/or added claims.

[1] Applicants argue, "compliance with the enablement requirement ... does not turn on whether an example is disclosed" and cite MPEP 2164.02 in support of this position (e.g., see 11/20/2003 Response, page 13, paragraph 3).

[2] Applicants argue that they provide both general and specific guidance (e.g., see 11/20/2003 Response, page 13, paragraph 4).

[3] Applicants argue that marker groups, hapten molecules, solid phase binding groups were well known in diagnostic assays and thus provide the necessary expertise to extend Applicants' four examples to an infinite number of compounds (e.g., see 11/20/2003 Response, page 13, last paragraph).

[4] Applicants argue that they only need to disclose one example in the present case to be entitled to an infinite number of methods and cite MPEP 2164.01(b) in support of their position (e.g., see 11/20/2003 Response, page 14, first full paragraph).

[5] Applicants argue that the Tam reference provides support that marker groups are well known in the art and thus "need not be described" (e.g., see 11/20/2003 Response, page 13, second full paragraph).

This is not found persuasive for the following reasons:

[1] The Examiner agrees with the rule set forth in MPEP 2164.02, but not its application as set forth by Applicants in the present case. Here, Applicants have provided neither a "representative number of examples" nor a "statement applicable to the genus as a whole" and, as a result, this rule only serves to further show that Applicants were not enabled (e.g., see enablement rejection above).

[2] This assertion is wholly unsubstantiated and is not commensurate in scope with the infinite number of compounds that are produced by the claimed method.

[3] The Examiner contends that although some marker molecules, hapten molecules, solid phase binding groups were known in the art only a few examples of conjugates using these groups were published and/or in use (e.g., see art rejections below). When there is little to no disclosure in the instant specification of the starting materials or conditions under which the

claimed process can be carried out, this failure cannot be rectified by asserting that all disclosure related to the process is within the skill of the art. *Genentech Inc. v. Novo Nordisk A/S* (CA FC) 42 USPQ2d 1001 (3/13/1997).

[4] The Examiner contends that their disclosure is not "representative" as indicated in the rejection above i.e., a method for producing a couple of compounds is not "representative" of a method for producing an infinite number of diverse structures. Thus, Applicants disclosure fails under MPEP 2164.01(b).

[5] The Examiner contends that the level of skill in the art is but one factor to be considered in the In re Wands analysis and as outlined in the rejection above the majority of Wands factors favor a conclusion for non-enablement (e.g., Applicants have not even refuted Wands factors 1-2 and 6-7 are also clearly in favor of a non-enablement conclusion). In addition, the Tam reference only applies to Marker groups and not haptens, solid-phase binding groups or reactive groups and thus only provides modest support for Wands factors 3 and 5. Furthermore, Applicants did not even address the issue of unpredictability in the prior art as set forth in Riley et al. and thus have implicitly conceded that the art is inherently unpredictable with regard to the haptens.

Where do the specification and/or prior art teach a person of ordinary skill how to chemically link an "unidentified" hapten (as disclosed by Riley et al.) to a synthetic carrier? What specific chemical reactions should be used to attach the carrier to the "unidentified" functional groups of the haptens? How will a person of skill in the art know whether a hapten will retain is ability to act as a hapten when it is bound to a carrier? Clearly, the specification is not enabled for ***all*** haptens.

In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved. See *In re Fisher*, 57 CCPA 1099,427 F.2d 833,839,166 USPQ 18,24(1970). Additionally, the Board has held on the issue of unpredictability that "... the unpredictability of an art area alone may be enough to create a reasonable doubt as to the accuracy of statements in the specification." *Ex parte Singh*, 17 U.S.P.Q.2d 1714,1716 (B.P.A.I. 1990). The Examiner maintains that the invention encompasses art that is inherently unpredictable and, consequently, the specification does not provide enablement for the full scope of the claims.

The question at hand is whether applicant has taught how to ***make and use*** the full scope of the claimed invention. Note that there must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and use the invention ***as broadly as it is claimed***. *In re Vaeck*, 947 F.2d 488, 496 & n.23, 20 USPQ2d 1438, 1445 & n.23 (Fed. Cir. 1991). The examiner's position is that the instant specification does not provide the necessary direction and guidance and the level of skill in the art was not such that a person of ordinary skill in the art would know how to make and use the invention as broadly as it is claimed. Also, see MPEP 2172.01

Accordingly, the Enablement rejection cited above is hereby maintained.

Claim Rejections - 35 USC § 112, second paragraph

13. Claims 1, 2, 5, 8, 17, 24 and 31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claims 1, 2, 5, 8, 17, 24 and 31 are rejected because the "solid phase binding groups" in these claims are not defined with any chemical or physical characteristic, but only by functional properties. A claim to a material defined solely in terms of what it can do, or a property thereof, does not particularly point out the claimed invention. A person of skill in the art cannot immediately envision all the possible chemical structures for a peptide with this function. Thus, the metes and bounds of the claimed invention cannot be determined. See *ex parte Pulvari* (POBA 1966) 157 USPQ 169. Here, it is not clear what the Applicants mean by the "solid phase binding groups" because any group (e.g., amino, carboxylate, etc) can be used to bind to a solid support. Thus, the metes and bounds of the claimed invention cannot be determined.

B. Claims 1, 2 and 8 recite, the term "predetermined positions." It is not clear on what basis the applicant determines such "predetermined" positions. Depending on the number of monomeric units in the conjugate, there are many possible positions and combination of positions to add further monomeric units to the conjugate. Applicants are requested to clarify. Therefore, the metes and bounds of the claimed invention cannot be determined.

Response

14. Applicant's arguments directed to the above 35 U.S.C. 112, second paragraph rejections were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or newly amended arguments.

A. Applicants argue that the term has a well-known meaning in the art as exemplified by the exhibits and that the specification provides an adequate definition at page 9, lines 5-16 (e.g., see 10/20/2003 Response, page 15, paragraph 1-2).

This is not found persuasive for the following reasons:

The Examiner contends that the term "solid phase binding group" is not defined in Applicants' exhibits. Furthermore, Applicants' specification does not provide a definition for the term (e.g., page 9, lines 8-16 do not even discuss the term and lines 5-8 only disclose preferred examples i.e., these lines do not provide a definition). Applicants state that the "solid phase binding group" refers to "groups that can be immobilized to a solid phase during a diagnostic assay", but the specification does not provide support for this statement.

B. Applicants argue that the term "predetermined positions" refers to "the controlled, defined, and reproducible introduction of moieties ... at specific positions in a carrier, which are selected in advance of introduction by an operator performing the synthesis ... [which] is quite distinct from the type of random or statistical attachment of moieties that

would result if the moieties were introduced in the presence of multiple equivalent reaction sites" and cite the specification at pages 6 and 11 in support of this position (e.g., see 10/20/2003 Response, page 15, paragraph 3).

This is not found persuasive for the following reasons:

The Examiner contends that although the specification does mention the term "predetermined positions" on pages 6 and 11 of the specification, it does not provide the definition that Applicants have set forth in their arguments and, as a result, the metes and bounds of the claimed invention still cannot be determined. In addition, neither Applicants' exhibits nor the prior art remedy this deficiency.

Accordingly, the 35 U.S.C. 112, second paragraph rejections cited above are hereby maintained.

Claim Rejections - 35 USC § 102

15. Claims 1-17, 19-24 and 26-31 are rejected under 35 USC 102(b) as being anticipated by Tam (US Patent No. 5,229,490) (Date of patent is **July 20, 1993**).

For ***claims 1-2 and 8***, Tam (see entire document) discloses methods for making a multiple antigen peptide system (see Tam, abstract), which anticipates claims 1, 2 and 8. For example, Tam discloses forming a carrier on a solid phase by linking together monomeric units (e.g., see Tam, Example 1 wherein an octabranched matrix core with peptide antigen was synthesized by a solid-phase procedure on a Boc-βAla-OCH_2-Pam resin using lysine monomeric units; see also claims 1 and 8, step (a)). In addition, Tam discloses introducing into the carrier at predetermined positions 1-10 additional

monomeric units covalently bound to hapten molecules (e.g., see Example 2 wherein 8 "Asn-Ala-Asn-Pro" are added to the carrier to produce the (Asn-Ala-Asn-Pro)$_8$-MAP(NP-16MAP); see also Table 1 wherein other haptens are disclosed; please note that the positions are "predetermined" because they involve addition only to the terminal lysines and not the internal lysines or the glycine). Tam also disclose an additional 1-10 monomeric units covalently bound to marker groups or solid phase binding groups. Although Tam does not provide a picture of the additional marker groups attached to the carrier, Tam does explicitly state that a different hapten group than those bound to the dendritic termini can replace the "core" glycine and can further be labeled with a fluorescent label like fluorescein (e.g., see column 8, last paragraph, "the free glycine could be ... replaced with, a peptide antigen which may be ... different from the other peptide antigens on the branches of the dendritic polymer"; see also column 10, lines 40-55, "The products of the invention may be employed in various diagnostic tests ... For such testing the diagnostic moiety [i.e., the hapten] joined to the dendritic polymer [i.e., the carrier] may be labeled with a detectable label [i.e., a marker molecule] ... includ[ing] fluorescent labels such as fluorescein, rhodamine or auramine ... Methods for labeling are well known and need not be described"; please note that the "predetermined" position is the addition of a labeled peptide to the glycine position as opposed to the terminal lysines). Tam also discloses that the conjugate comprises a minimum of 5 and a maximum of 100 monomeric units selected from the group consisting of nucleotides, peptidic nucleic acids and amino acids (e.g., see Tam, Example 2 wherein a core of 8 lysines is attached to 8 tetrapeptides to make a conjugate with $(8 + (8 \times 4))$ monomers + 1

glycine = 43 monomer or if glycine is substituted for another labeled tetrapeptide as mentioned above 42 + 4 monomers or 46 monomers total), which is between 5 and 100. Finally, Tam discloses amino acid monomers with lysine amino side chain attachments. Tam also disclose the use of various orthogonal protecting groups including, Boc, Fmoc, etc. to insure "pre-determined" positioning (e.g., see Example 1).

For ***claim 4***, Tam discloses the addition of 8 haptens or 9 haptens if a different hapten is added to the glycine as indicated above (e.g., see Tam, Figure 1; see also examples).

For ***claim 5***, Tam discloses primary lysine amino groups (e.g., see Figure 1; see also examples).

For ***claims 6-7***, Tam discloses selectively cleavable acid-labile protecting groups for primary amines (e.g., see Tam, column 8, lines 9-16, "This makes it possible to protect either of the amino groups of lysine by the orthogonal protection method").

For ***claims 9-11***, Tam discloses haptens that range from ~4 to ~20 amino acids (e.g., see Examples, see also Table 1).

For ***claims 12-13, 17, 19-20, 24, 26-27 and 31***, Tam discloses, for example, vitamins (e.g., biotin is a vitamin and thus would be immediately envisioned) and steroids (e.g., see column 10, line 32), which would also fall under the analogues/derivatives category (e.g., see 35 U.S.C. 112, second paragraph rejection below).

For ***claims 14-15, 21-22 and 28-29***, Tam discloses peptides derived from various pathogenic organisms including HIV-1 (e.g., see Table 1, reference 15).

For ***claims 16, 23 and 30***, Tam discloses, for example, the fluorescent label fluorescein (e.g., see column 10, line 49).

Response

16. Applicant's arguments directed to the above 35 U.S.C. § 102 rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

[1] Applicants argue, "the Tam reference does not teach or suggest a carrier that simultaneously contains both a peptide antigen (e.g., a hapten molecule) and a diagnostic moiety (e.g., a marker group), as required ... it is evident that the diagnostic agent described in Tam is intended to be used as an alternative to the peptide antigen and that the carriers described therein would not contain both a peptide antigen and a detectable marker at the same time" (e.g., see 10/20/2003 Response, page 17, second full paragraph).

[2] Applicants argue, "the Tam reference does not teach or suggest a carrier that simultaneously contains both a peptide antigen (e.g., a hapten molecule) and a solid phase binding group" and that even if assuming arguendo the Gly-OH did qualify as a solid phase binding group it would not be at a "predetermined position" as required by the claims (e.g., see 10/20/2003 Response, paragraph bridging pages 17-18).

This is not found persuasive for the following reasons:

[1] The Examiner respectfully contends that this is not a fair interpretation of the Tam reference. Nowhere in the reference does it state that the diagnostic moieties (e.g., the marker molecules) would replace "all" of the peptide antigens (e.g., the hapten molecules) as Applicants contend. Rather, the better view is that the marker molecules replace only one (or a few) of the hapten molecules (depending on the signal intensity required) because the conjugate could not function as a "diagnostic agent" if "all" the peptide antigens were replaced. For example, if all of the hapten molecules were replaced by marker molecules then no signal would be generated for any analyte (e.g., haptens) and, as a result, the conjugate would be completely useless because no analyte/signal correlation would exist. Thus, Applicants interpretation of the reference is unreasonable. Furthermore, Applicants arguments read on the interpretation that the marker molecule could be attached to the hapten itself. In addition, Applicants have already noted that labeling conjugates using a wide variety of linkages would be immediately envisioned and is well known in the art (e.g., see 11/20/2003 Response, page 14, paragraph 2).

[2] Applicant's argument that the marker groups are not taught with the carrier and the hapten because "there is no teaching as to how such labels should be attached to the dendritic polymers, nor indeed at what positions they should be attached" is not found persuassive. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., "how such labels should be attached" and "at what positions they should be attached") are not recited in the rejected claim(s). The claims simply do not address the issue of "how" the labels are to be attached to the carrier. Furthermore, the position at which the labels should be attached is also not addressed by the claims because the "predetermined" locations of the monomers that covalently bind to the

marker groups are vague and indefinite (see 35 USC 112, Second Paragraph Rejection above). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

In addition, the claims states that the "1-10 additional monomeric units can be covalently bound to "marker groups OR solid phase binding groups" i.e., marker groups are not even required. Clearly, the peptide antigen linked dendrimer contains a "solid phase binding group" since it was cleaved from a solid phase resin (see Tam et al, Example 2). Therefore, the claims would still be anticipated even if it could be shown that the "marker groups" were not anticipated (see also Tam et al, Figure 1, wherein the Gly-OH could be bound to a solid phase resin).

Accordingly, the 35 U.S.C. 102 rejection cited above is hereby maintained.

New Rejections

Claims Rejections - 35 U.S.C. 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

136. Claims 1, 2 and 8-32 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed had possession of the claimed invention. This is a new matter rejection.

Claims 1, 2 and 8-32 were amended and/or added in the 10/20/2003 Response. However, Applicants do not provide support for the broader "combinations thereof" terminology found in the rejected claims. If applicant believes this rejection is in error, applicant must disclose where in the specification support for this amendment can be found in accordance with MPEP § 714.02.

Claims Rejections - 35 U.S.C. 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

17. Claims 12-13, 18-20, 24, 26-27 and 31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

AA. For ***claims 18, 24 and 31***, the metes and bounds of the "*biotin analogues*" cannot be determined because applicants have only provided examples of molecules to be included and not a means for determining whether any given molecule (other than the examples) should be encompassed by the term. Thus, the metes and bounds of the claimed invention cannot be determined.

BB. For ***claims 12-13, 19-20 and 26-27***, the metes and bounds of the "derivatives" cited therein (e.g., quinine, estradiol, etc.) cannot be determined because applicants have only provided examples of such molecules and not a means for determining whether any

given molecule (other than the examples) should be encompassed by the term. Thus, the metes and bounds of the claimed invention cannot be determined.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (571) 272-0808. The examiner can normally be reached Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is (571) 272-0811.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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BENNETT CELSA